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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 10/625,085   | 07/23/2003  | Sabine Gratzer       | DEAV2002/0051US NP  | 5941             |
| 5487   | 7590        | 02/27/2006           | EXAMINER            |                  |
| ROSS J. OEHLER<br>AVENTIS PHARMACEUTICALS INC.<br>ROUTE 202-206<br>MAIL CODE: D303A<br>BRIDGEWATER, NJ 08807 |             |                      | JOIKE, MICHELE K    |                  |
|  |             | ART UNIT             |                     | PAPER NUMBER     |
|  |             | 1636                 |                     |                  |
| DATE MAILED: 02/27/2006  |             |                      |                     |                  |

Please find below and/or attached an Office communication concerning this application or proceeding.

|                              |                                     |                     |  |
|------------------------------|-------------------------------------|---------------------|--|
| <b>Office Action Summary</b> | <b>Application No.</b>              | <b>Applicant(s)</b> |  |
|                              | 10/625,085                          | GRATZER ET AL.      |  |
|                              | Examiner<br>Michele K. Joike, Ph.D. | Art Unit<br>1636    |  |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 23 July 2003.  
 2a) This action is FINAL.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-18 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 1-18 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
     1. Certified copies of the priority documents have been received.  
     2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
     3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |   |   |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|   | 6) <input type="checkbox"/> Other: _____                                    |

**DETAILED ACTION**

***Priority***

Applicant is advised of possible benefits under 35 U.S.C. 119(a)-(d), wherein an application for patent filed in the United States may be entitled to the benefit of the filing date of a prior application filed in a foreign country.

Receipt is acknowledged of German application 10233516.8-41 filed on July 23, 2002 and submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. It is noted that no English translation has been filed.

It is noted that this application appears to claim subject matter disclosed in prior Application No. 60/430,258 filed December 2, 2002. A reference to the prior application must be inserted as the first sentence(s) of the specification of this application or in an application data sheet (37 CFR 1.76), if applicant intends to rely on the filing date of the prior application under 35 U.S.C. 119(e), 120, 121, or 365(c). See 37 CFR 1.78(a). For benefit claims under 35 U.S.C. 120, 121, or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of all nonprovisional applications. If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference to the prior application must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted

during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

If the reference to the prior application was previously submitted within the time period set forth in 37 CFR 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 CFR 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 CFR 1.78(a) and the surcharge

under 37 CFR 1.17(t) are not required. Applicant is still required to submit the reference in compliance with 37 CFR 1.78(a) by filing an amendment to the first sentence(s) of the specification or an ADS. See MPEP § 201.11.

This application claims benefit to provisional application No. 60/430,258, filed on 12/02/02, in a language other than English. An English translation of the non-English language provisional application and a statement that the translation is accurate must be filed in provisional application No. 60/430,258. See 37 CFR 1.78(a)(5). The translation required by 37 CFR 1.78(a)(5) is missing. Accordingly, applicant must supply 1) the missing translation in provisional application No. 60/430,258 and 2) in the present application, a confirmation that the translation and statement were filed in the provisional application. If 1) and 2) are not filed (or the benefit claim withdrawn by the filing of an amendment or Supplemental Application Data Sheet) prior to the expiration of the time period set in this Office action, the present application will be abandoned. See 37 CFR 1.78(a)(5)(iv).

### ***Specification***

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: Method for identifying substances capable of modulating the activity of a target molecule.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 3-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In claims 1 and 3-18, it is unclear what relationship the reporter gene has to the target molecule, and how a change in reporter activity relates to whether an agent modulates activity of a reporter molecule. In claims 14 and 15, the term "intermediary molecule" is indefinite, however, Examiner is interpreting the term to mean any molecule that is not the target molecule or the end product for purposes of examination.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5, 12-14 and 16-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Pausch.

Applicant claims a method of identifying an agent that modulates the activity of a target molecule by contacting a cell and modulating a target molecule, wherein said cell also comprises a reporter gene. After contact by agent, cell propagation and reporter

activity are measured. The target molecule affects the reporter gene, and is further limited to a heterologous molecule and can be a nucleic acid or polypeptide. The target molecule affects cellular propagation indirectly or through an intermediary molecule. . The target molecule can also affect the reporter gene and cellular propagation directly. The reporter gene produces an enzyme. The cell is a yeast cell, specifically *S. cerevisiae*.

Pausch (TIBTECH 15: 487-494, 1997, specifically Fig. 1b and p. 490) teaches a method of identifying an agent that modulates the activity of a target molecule by contacting a cell and modulating a target molecule, wherein an agent, somostatin, modulates a target molecule, Sst2 (a heterologous receptor), which induces a FUS1-HIS3 reporter in a *S. cerevisiae* cell, causing expression of the His3 enzyme. Reporter activity is measured by growth on medium lacking histidine. A deletion of the FAR1 gene prevents cell cycle arrest, thereby affecting cell propagation. Sst2 activates a Map kinase pathway including Fus3, which activates FAR1. However, FAR1 is deleted, so Sst2 affects cell propagation indirectly and through an intermediary molecule, Fus3. Fus3 is not able to activate FAR1, therefore there is cell growth. In another embodiment, Fus3 activates the FAR1 gene, which causes cell cycle arrest. However, deletion of the FAR1 gene prevents cell cycle arrest, therefore, Fus3 directly affects cell propagation. As such, Pausch anticipates each one of these claims.

Claims 1, 5, 10-11 and 18 are rejected under 35 U.S.C. 102(b) as being anticipated by Crossin et al.

Applicant claims a method of identifying an agent that modulates the activity of a target molecule by an agent contacting a cell and modulating a target molecule, wherein said cell also comprises a reporter gene. After contact by agent, cell propagation and reporter activity are measured. The reporter gene produces an enzyme. Measuring reporter activity comprises disrupting the cell by permeabilizing the membrane, or destroying the membrane. They also claim a second cell with a target molecule and reporter gene. After contact by agent, cell propagation and reporter activity are measured.

Crossin et al (PNAS 94: 2687-2692, 1997, specifically Abstract, Introduction, last paragraph, Exptl. Procedures, 2<sup>nd</sup>, 7<sup>th</sup> and last paragraph and Figure 4) teach a method of identifying an agent that modulates the activity of a target molecule by contacting a cell and modulating a target molecule, wherein an agonist, N-CAM, modulates a target molecule, GRE, which induces a luciferase reporter. N-CAM inhibits cell proliferation. In measuring luciferase activity, cells were lysed. They also teach a second cell with a second target molecule, CM-V and a second reporter beta-galactosidase. N-CAM is the agonist. As such, Crossin et al anticipate each one of these claims.

*include claim 8 here*  
Claims 1-7, 9-11 and 13-14 are rejected under 35 U.S.C. 102(b) as being anticipated by Keating et al. X

Applicant claims a method of identifying an agent that modulates the activity of a target molecule by an agent contacting a cell and modulating a target molecule, wherein said cell also comprises a reporter gene. After contact by agent, cell propagation and reporter activity are measured. The reporter gene produces an enzyme, and the

substrate of the enzyme is added after a delay, specifically at least one cell cycle.

Measuring reporter activity comprises disrupting the cell by permeabilizing the membrane, or destroying the membrane.

Keating et al (Oncogene 20: 4281-4290, 2001, specifically Introduction, p. 4282 and Materials & Methods, 1<sup>st</sup> and 6<sup>th</sup> paragraphs) teach a method of identifying an agent that modulates the activity of a target molecule by contacting a cell and modulating a target molecule, wherein an agent, EGF, modulates a target molecule, ATM (a heterologous kinase), which induces a luciferase reporter. ATM is known to be involved in cell cycle control (see Abstract & Introduction). Cells were incubated with EGF for 16 hours before cells extracts were prepared. EGF was added during log phase, therefore at least one or two cell cycles have occurred. Firefly luciferase substrate (LARII) was added and reporter activity was measured using a Dual Luciferase Assay. As such, Keating et al anticipate each one of these claims.

***Allowable Subject Matter***

No claims are allowed.

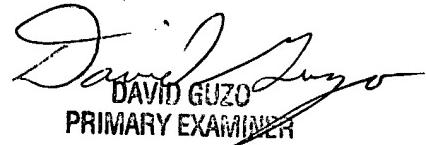
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michele K. Joike, Ph.D. whose telephone number is 571-272-5915. The examiner can normally be reached on M-F, 9:00-6:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D. can be reached on 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michele K Joike, Ph.D.  
Examiner  
Art Unit 1636



DAVID GUZO  
PRIMARY EXAMINER